FORM-PTO-1390 (Rev. 9-2001) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: 003300-872

U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.5): unassigned 09/980784

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/SE00/01179	7 June 2000	9 June 1999

TITLE OF INVENTION
ANTIBODIES TO NUCLEUS PULPOSUS IN DISC HERNIATION, DIAGNOSTIC KIT, MEDICAL PREPARATION AND TREATMENT

APPLICANT(S) FOR DO/EO/US
KJELL OLMARKER AND BJÖRN RYDEVIK

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. ☐ The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☒ is attached hereto (required only if not communicated by the International Bureau).
   b. ☒ has been communicated by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☐ is attached hereto.
   b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. ☐ are attached hereto (required only if not communicated by the International Bureau).
   b. ☐ have been communicated by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). (Signed Declaration will follow)
10. ☐ An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 to 20 below concern document(s) or information included:

11. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A FIRST preliminary amendment.
14. ☐ A SECOND or SUBSEQUENT preliminary amendment.
15. ☐ A substitute specification.
16. ☐ A change of power of attorney and/or address letter.
17. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
18. ☐ A second copy of the published international application under 35 U.S.C. 154(d)(4).
19. ☐ A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. ☒ Other items or information: A certified copy of Swedish Application No. 9902155-2 filed 9 June 1999 was submitted during the international phase of prosecution. Thus the claim for priority has been perfected.

21839

JC13 Rec'd PCT/PTO 0 6 DEC 2001

U.S. APPLICATION NO. (If known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
Unassigned 09/980784	PCT/SE00/01179	003300-872

21. ☒ The following fees are submitted:

	CALCULATIONS	PTO USE ONLY
Basic National Fee (37 CFR 1.492(a)(1)-(5)):		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO $1,040.00 (960)		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO $890.00 (970)		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO $740.00 (958)		
International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) $710.00 (956)		
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) $100.00 (962)		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 1,040.00	
Surcharge of **$130.00 (154)** for furnishing the oath or declaration later than 20 ☐ 30 ☐ months from the earliest claimed priority date (37 CFR 1.492(e)).	$ --	

Claims	Number Filed	Number Extra	Rate		
Total Claims	8 -20 =	0	X$18.00 (966)	$ --	
Independent Claims	8 -3 =	5	X$84.00 (964)	$ 420.00	
Multiple dependent claim(s) (if applicable)			+ $280.00 (968)	$ --	
TOTAL OF ABOVE CALCULATIONS =				$ 1,460.00	
Reduction for 1/2 for filing by small entity, if applicable (see below).			+	$ 730.00	-
SUBTOTAL =				$ 730.00	
Processing fee of **$130.00 (156)** for furnishing the English translation later than 20 ☐ 30 ☐ months from the earliest claimed priority date (37 CFR 1.492(f)).			+	$ --	
TOTAL NATIONAL FEE =				$ 730.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00 (581)** per property			+	$ --	
TOTAL FEES ENCLOSED =				$ 730.00	
				Amount to be refunded:	$
				charged:	$

a. ☒ Small entity status is hereby claimed.

b. ☒ A check in the amount of $ 730.00 to cover the above fees is enclosed.

c. ☐ Please charge my Deposit Account No. 02-4800 in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.

d. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 02-4800. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

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22,030
REGISTRATION NUMBER

December 6, 2007
DATE

Patent
Attorney's Docket No. 003300-872

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	**BOX PCT**
	Attention: DO/EO/US
KJELL OLMARKER et al.	
	Group Art Unit: (unassigned)
Application No.: (unassigned)	
	Examiner: (unassigned)
Filed: December 6, 2001	
For: ANTIBODIES TO NUCLEUS PULPOSUS IN DISC HERNIATION, DIAGNOSTIC KIT, MEDICAL PREPARATIONS AND TREATMENT	

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This is a national phase filing of International Application No. PCT/SE00/01179, filed June 7, 2000.

Please amend the Application as indicated.

IN THE ABSTRACT:

Please add the Abstract of the Disclosure that is provided on a separate sheet.

IN THE CLAIMS:

Kindly replace Claims 1 to 8 as follows:

1. (Amended) Kit for diagnosing disc herniation,

comprising antigens from nucleus pulposus cells for determining the presence of antibodies to nucleus pulposus.

2. (Amended) A method for the treatment of disc herniation comprising administering an effective amount of an anti-antibody to antibodies of nucleus pulposus cells to a patient in need of such treatment.

3. (Amended) A method for the treatment of disc herniation comprising administering an effective amount of a false antibody to nucleus pulposus cells to a patient in need of such treatment, which false antibody is able to bind to and block the antigen in such a way that an immunological reaction is inhibited.

4. (Amended) A method or for the diagnosis or treatment of disc herniation comprising administering any effective amount of soluble antigens from nucleus pulposus cells to a patient in need of treatment.

5. (Amended) A method for treating disc herniation comprising administering to a patient in need of treatment a therapeutically efficient amount of a compound that prevents the binding of serum antibodies to nucleus pulposus cells to bind to nucleus pulposus.

6. (Amended) A method for treating disc herniation comprising administering a therapeutically effective amount of an anti-antibody to antibodies of nucleus pulposus cells.

7. (Amended) A method for treating disc herniation comprising administering a therapeutically effective amount of a false antibody to nucleus pulposus, which false antibody is able to bind to and block the antigen in such a way that an immunological reaction is inhibited.

8. (Amended) A method for treating disc herniation comprising administering a therapeutically effective amount of soluble antigens from nucleus pulposus cells.

REMARKS

The present Amendment provides an Abstract of the Disclosure on a separate sheet and modifies the claim format.

An Information Disclosure Statement is being filed concurrently herewith.

The examination and allowance of the Application are respectfully requested.

Respectfully submitted,

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Date: December 6, 2001

Attachment to Preliminary Amendment dated December 6, 2001

Marked-up Claims -

1. (Amended) Kit for diagnosing disc herniation,

[characterized in that it comprises] comprising antigens from nucleus pulposus cells for determining [an optional] the presence of antibodies to nucleus pulposus.

2. (Amended) [The use of an anti-antibody to antibodies to nucleus pulposus cells in the manufacture of a medicament] A method for the treatment of disc herniation comprising administering an effective amount of an anti-antibody to antibodies of nucleus pulposus cells to a patient in need of such treatment.

3. (Amended) [The use of a false antibody to nucleus pulposus cells in the manufacture of a medicament] A method for the treatment of disc herniation comprising administering an effective amount of a false antibody to nucleus pulposus cells to a patient in need of such treatment, which false antibody is able to bind to and block the antigen in such a way that an immunological reaction is inhibited.

4. (Amended) [The use of soluble antigens from nucleus pulposus cells in the manufacture of a medicament or a diagnostic means] A method or for the diagnosis or treatment of disc herniation comprising administering any effective amount of soluble antigens from nucleus pulposus cells to a patient in need of treatment.

Attachment to Preliminary Amendment dated December 6, 2001

Marked-up Claims -

5. (Amended) [Method] A method for treating disc herniation[, whereby] comprising administering to a patient in need of treatment a therapeutically efficient amount of a compound that prevents the binding of serum antibodies to nucleus pulposus cells to bind to nucleus pulposus.

6. (Amended) [Method] A method for treating disc herniation[, whereby] comprising administering a therapeutically [efficient] effective amount of an anti-antibody to antibodies of nucleus pulposus cells [is administered].

7. (Amended) [Method] A method for treating disc herniation[, whereby] comprising administering a therapeutically [efficient] effective amount of a false antibody to nucleus pulposus [is administered], which false antibody is able to bind to and block the antigen in such a way that an immunological reaction is inhibited.

8. (Amended) [Method] A method for treating disc herniation[, whereby] comprising administering a therapeutically [efficient] effective amount of soluble antigens from nucleus pulposus cells [is administered].

TITLE

ANTIBODIES TO NUCLEUS PULPOSUS IN DISC HERNIATION, DIAGNOSTIC KIT, MEDICAL PREPARATIONS AND TREATMENT

DESCRIPTION

Technical field

The present invention relates the use of serum antibodies for the diagnosis and treatment of disc herniation with resulting nerve root pain in the cervical and lumbar spine such as sciatica.

The object of the present invention is to obtain improved methods in diagnosis and treatment of nerve root pain such as sciatica and other radiculopathies related to disc herniation in the cervical or lumbar spine.

Background of the invention

The exact pathophysiological mechanisms leading to sciatica in relation to herniation of intervertebral discs are not fully understood. Recently it was demonstrated that the nucleus pulposus (the viscous component of the intervertebral disc that leaks out into the spinal canal in case of disc herniation) may induce structural and functional changes in the adjacent nerve root (1-14). Also, it has been shown that nerve roots experimentally exposed to nucleus pulposus become sensitive to mechanical deformation thereby producing pain (8,13). Certain pro-inflammatory cytokines, produced by the nucleus pulposus cells, have been defined as being responsible for inducing these effects (10). However, there is both clinical and experimental evidence which may suggest that also immunologic mechanisms may be present to a certain extent. It has been suggested that, since the nucleus pulposus is secluded from the immune-system from birth, being a non-vascularized tissue, the immune system has not regarded the nucleus pulposus as "self" during early embryonic stages, but would instead consider the nucleus pulposus as "non-self" later in life (15-22). At disc herniation, possible antigens in the nucleus pulposus might thus be presented to the immune system and there would be an auto-immune reaction induced towards these antigens. The reaction would mainly involve the nucleus pulposus, but the substances might also induce changes in the adjacent nerve roots secondary to this reaction. These suggested substances would most likely be the same pro-inflammatory cytokines as previously being defined as

inducing nerve root injury. There is reason to believe that such mechanisms also relates to radiculopathies in the upper extremities due to disc herniation in the cervical spine. However, no one has previously been able to demonstrate the presence of antibodies in serum towards the nucleus pulposus of the same individual.

In order to isolate and show the presence of antibodies towards nucleus pulposus cells the following experiments and tests were conducted.

Material and methods

1) Culture of nucleus pulposus cells:

One pig weighing 26 kg was anaesthetized with an intra muscular injection of 20 mg/kg body weight of Ketalar^{R} (ketamine 50 mg/ml, Parke-Davis, Morris Plains, NJ) and an intravenous injection of 4 mg/kg body weight of Hypnodil^{R} (methomidate chloride 50 mg/ml, AB Leo, Helsingborg, Sweden) and 0,1 mg/kg body weight of Stresnil^{R} (azaperon, 2 mg/ml, Janssen Pharmaceutica, Beerse, Belgium).

Approximately 20 ml of blood were collected and allowed to coagulate at room temperature. It was then centrifuged and the supernatant (serum) was stored at 80°C in a refrigerator.

After induction of anaesthesia, the pig was killed by an overdose of potassium chloride. The lumbar and lower part of the thoracic spine was removed en bloc. The spine was cleansed from muscles and tendons. Under sterile conditions the discs were incised and the nucleus pulposus was harvested. The nucleus pulposus (NP) was washed once in Ham's F12 medium (Gibco BRL, Paisley, Scotland).The NP from discs were placed in a test tube with Ham's F12 medium and centrifuged. The remaining pellet was dissolved in 6 ml of Ham's F12 with 3 ml of trypsine 2.5 % in a 75 cm^2 culture flask for 30 minutes at 37°C. Then 6 ml of Ham's F12 with 12 mg of collagenase (Sigma Cat. No. C9407) were added. After 3.5 hrs at 37°C the content of the culture flask was transferred to a test tube and centrifuged. The separated NP-cell pellets were suspended in DMEM/F12 1:1 medium (Gibco BRL, Paisley, Scotland) supplemented with 1% L-glutamine (200 mM, Gibco BRL, Paisley, Scotland), 50 µg/ml gentamycine sulphate (Gibco BRL, Paisley, Scotland) and 10% foetal calf serum

(FCS, Gibco BRL, Paisley, Scotland). Fungizone 2 µg/ml and α-ascorbic acid 50 µg/ml was added. The cells were cultured in 25 cm^2 flasks (Costar, Cambridge, MA), at 37°C and 5% CO_2 in air for 3-4 weeks . After 2 weeks the cells were transferred to 4-chamber polystyrene vessel tissue culture treated glass slides (Becton Dickinson Labware, Franklin Lakes, NJ). Following 3 days of culture the slides were used for the assessment as will be described below.

2) Culture of fibroblasts

A 2x2 cm big piece of the skin was harvested at the same time as the nucleus pulposus under sterile conditions. The dermis of the skin was cut in small pieces and put in spinner bottles with 10 ml of collagenase solution (0.8 mg/ml, Sigma Chemical, St. Louis, MO, in Ham's F12 medium) for 90 minutes in 37°C water bath. The separated fibroblasts were centrifuged and transferred to 75 cm^2 tissue culture flasks (Costar, Cambridge, MA), with DMEM/F12 1:1 medium supplemented as above for NP-cells.

3) Pretreatment of the serum

The cultured fibroblasts were liberated from the culture flasks by treatment of 0.125% trypsine solution (Gibco BRL, Paisley, Scotland) and added to the serum. The addition of fibroblasts was performed in order to eliminate the risk that antibodies in the serum which non-specifically would bind to cultured cells, would be applied to the nucleus pulposus cells. The test-tube was centrifuged and the supernatant collected (serum with remaining antibodies).

4). Assessment of the presence of antibodies in serum towards autologous nucleus pulposus cells

The culture slides with the cultured nucleus pulposus cells were fixed in acetone for 10 minutes and then dried in air. The slides were washed twice for 5 minutes in PBS (Phosphate Buffered Saline, Life Technologies Ltd., Paisley, Scotland) The slides were then treated with 0.3% H2O2 (Sigma Chemical, St. Louis, MO) for 30 minutes and then washed twice for 5 minutes in PBS. The slides were then exposed to standard freeze-dried milk (5% in PBS) for 30 minutes to block irrelevant antigens, and then washed twice for 5 minutes in PBS.

The cultured NP-cells were exposed to

a) one drop of the pretreated serum,

b) one drop of the pretreated serum diluted by PBS 1:40; or

c) not in serum at all, and

incubated for 1 hr at room temperature, and then washed twice for 5 minutes in PBS. The culture slides were then incubated with the secondary antibody (Peroxidase-Conjugated Rabbit Anti-Swine immunoglobulin, Code No. P164, Dako A/S, Glostrup, Denmark) for 30 minutes, and then washed twice for 5 minutes in PBS. The slides were finally developed with DAB (3,3'-diaminobenzidine, 10 mg in 5 ml PBS, and 17 µl H_2O_2 (3%), Sigma Chemical, St. Louis, MO) for 2 minutes, and then washed twice for 5 minutes in PBS. The specimens were dehydrated in a series of alcohol-dilutions and assessed by light microscopy.

Results

a) Pretreated serum

There was a clear staining of the cell membranes of the nucleus pulposus cells and also of the nuclei of the cells. This indicates the presence of specific antibodies towards the nucleus pulposus cells in serum from the same individual (autologous).

b) Pretreated serum at 1:40

There was a similar staining of the cells as for the concentrated serum, although not as pronounced.

c) Nucleus pulposus cells not exposed to serum

There was no staining of the cells and the cells were difficult to distinguish on the culture slides. This suggests that the secondary antibody (rabbit:anti-swine-immunoglobulin) did not non-specifically bind to the pig nucleus pulposus cells and that the staining of a) and b) was the result of the addition of specific antibodies from the serum.

Conclusion and comments

The following conclusion can be made from the present experiment:

- There are antibodies present in serum that specifically bind to nucleus pulposus cells of the

same individual

The following comments can be made from the present experiment

- From this study it can not be recognized if the antibodies are readily available in high concentrations in serum or if there had been an immunization to the nucleus pulposus in the pig. If there are antibodies already present in the serum, the antigen may be a potent antigen, comparable for instance to the MHC (Major Histocompatibility Complex)antigens.
- Regardless of the nature of the antigen one can suspect that the levels in serum may increase the levels of these antibodies in case of disc herniation and sciatica and therefore used as a diagnostic tool.
- At present the diagnosis of sciatica is made by patient history and radiologic findings. However, since it is known that almost 30% of the population without any complaints of sciatica also have disc herniations at radiological examinations, the radiologic diagnosis is less valuable (23-25). It has been suggested that disc herniations can be can be either active (symptoms) or inactive (no symptoms). Based on the findings in the present study it is assumed that an active disc herniation is related to inflammatory and immunologic changes, whereas the inactive disc herniation is a mere protrusion of disc tissue without triggering of the immune system. The lack of immunologic reaction might be based on either the nucleus pulposus still being isolated from the epidural space by remaining membranes or a less developed immunoreactivity of the patient, alternatively lack of sensitizing antigens in the disc cells.

The present invention can thus be used in the form of an antigen containing diagnostic kit for diagnosing disc herniation, in particular disc herniation leading to sciatica. Further the effects of serum antibodies towards the nucleus pulposus cells (NP-antibodies) can be neutralized in three ways. First the NP-antibodies can be inactivated by administering a specific antibody for such serum antibodies, an anti-antibody. Secondly, the effects of the NP-antibodies can be inhibited by administering a substance that is similar to the NP-antibody, a false antibody, and binds to the antigen in the nucleus pulposus in stead of the antibody, which false antibody is able to bind to and block the antigen in such a way that an immunological reaction is inhibited. Thirdly, soluble antigens corresponding to the NP-antibodies can be administered, thereby blocking the effects of the NP-antibodies. In such

ways the action of the NP-antibodies can be blocked since the NP-antibodies are prevented from binding to its antigen.

The compounds of the invention can be administered in a variety of dosage forms, e.g, orally, in the form of tablets, capsules, sugar or film coated tablets, liquid solutions; rectally, in the form of suppositories; parenterally, e.g., intramuscularly or by intravenous injection or infusion. The therapeutic regimen for the different clinical syndromes must be adapted to the type of pathology taken in to account, as usual, also the route of administration, the form in which the compound is administered and age, weight, and condition of the subject involved.

The oral route is employed, in general, for all conditions, requiring such compounds. In emergency cases preference is given to intravenous injection. For these purposes the compounds of the invention can be administered orally at doses ranging from about 20 to about 1500 mg/day. Of course, these dosage regimens may be adjusted to provide the optimal therapeutic response.

The nature of the pharmaceutical composition containing the compounds of the invention in association with pharmaceutically acceptable carriers or diluents will, of course, depend upon the desired route of administration. The composition may be formulated in the conventional manner with the usual ingredients. For example, the compounds of the invention may be administered in the form of aqueous or oily solutions or suspensions, tablets, pills, gelatine capsules (hard or soft ones)syrups, drops or suppositories.

Thus for oral administration, the pharmaceutical compositions containing the compounds of the invention are preferably tablets, pills or gelatine capsules, which contain the active substance together with diluents, such as lactose, dextrose, sucrose, mannitol, sorbitol, cellulose; lubricants, e.g., silica, talc, stearic acid, magnesium or calcium stearate, and/or polyethylene glycols; or they may also contain binders, such as starches, gelatine, methyl cellulose, carboxymethylcellulose, gum arabic, tragacanth, polyvinylpyrrolidone; disaggregating agents such as starches, alginic acid, alginates, sodium starch glycolate, microcrystalline cellulose; effervescing agents such a carbonates and acids; dyestoffs;

sweeteners; wetting agents, such as lecithin, polysorbates, laurylsulphates; and in general non-toxic and pharmaceutically inert substances used in the formulation of pharmaceutical compositions. The mentioned pharmaceutical compositions may be manufactured in known manners, e.g., by means of mixing, granulating, tableting, sugar-coating or film-coating processes. In the case film providing compounds can be selected to provide release in the right place in the intestinal tract with regard to absorption and maximum effect. Thus pH-dependent film formers can be used to allow absorption in the intestines as such, whereby different phthalate are normally used or acrylic acid/methacrylic acid derivatives and polymers.

The liquid dispersions for oral administration may be e.g., syrups, emulsion, and suspensions.

The syrups may contain as carrier, e.g., saccharose, or saccharose with glycerine and/or mannitol and/or sorbitol.

Suspensions and emulsions may contain as carrier, e.g., a natural gum, such as gum arabic, xanthan gum, agar, sodium alginate, pectin, methyl cellulose, carboxymethylcellulose, polyvinyl alcohol.

The suspension or solutions for intramuscular injections may contain together with the active compound, a pharmaceutically acceptable carrier, such as e.g., sterile water, olive oil, ethyl oleate, glycols,, e.g., propylene glycol, and if so desired, a suitable amount of lidocaine hydrochloride. Adjuvants for trigging the injection effect can be added as well.

The solutions for intravenous injection or infusion may contain as carrier, e.g., sterile water, or preferably, a sterile isotonic saline solution, as well as adjuvants used in the field of injection of active compounds.

The suppositories may contain together with the active compound, a pharmaceutically acceptable carrier, e.g., cocoa-butter polyethylene glycol, a polyethylene sorbitan fatty acid ester surfactant or lecithin.

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CLAIMS

1. Kit for diagnosing disc herniation,
characterized in that it comprises antigens from nucleus pulposus cells for determining an optional presence of antibodies to nucleus pulposus.

2. The use of an anti-antibody to antibodies to nucleus pulposus cells in the manufacture of a medicament for the treatment of disc herniation.

3. The use of a false antibody to nucleus pulposus cells in the manufacture of a medicament for the treatment of disc herniation, which false antibody is able to bind to and block the antigen in such a way that an immunological reaction is inhibited.

4. The use of soluble antigens from nucleus pulposus cells in the manufacture of a medicament or a diagnostic means for the diagnosis or treatment of disc herniation.

5. Method for treating disc herniation, whereby a therapeutically efficient amount of a compound that prevents the binding of serum antibodies to nucleus pulposus cells to bind to nucleus pulposus.

6. Method for treating disc herniation, whereby a therapeutically efficient amount of an anti-antibody to antibodies of nucleus pulposus cells is administered.

7. Method for treating disc herniation, whereby a therapeutically efficient amount of a false antibody to nucleus pulposus is administered, which false antibody is able to bind to and block the antigen in such a way that an immunological reaction is inhibited.

8. Method for treating disc herniation, whereby a therapeutically efficient amount of soluble antigens from nucleus pulposus cells is administered.

COMBINED DECLARATION AND POWER OF ATTORNEY FOR UTILITY PATENT APPLICATION	Attorney's Docket No. 003300-872

As a below-named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name;

I BELIEVE I AM THE ORIGINAL, FIRST AND SOLE INVENTOR (if only one name is listed below) OR AN ORIGINAL, FIRST AND JOINT INVENTOR (if more than one name is listed below) OF THE SUBJECT MATTER WHICH IS CLAIMED AND FOR WHICH A PATENT IS SOUGHT ON THE INVENTION ENTITLED:

ANTIBODIES TO NUCLEUS PULPOSUS IN DISC HERNIATION, DIAGNOSTIC KIT,

MEDICAL PREPARATIONS AND TREATMENT

the specification of which

(check one) ☐ is attached hereto;

☒ was filed on June 7, 2000 as

Application No. PCT/SE00/01179

and was amended on _____;
(if applicable)

I HAVE REVIEWED AND UNDERSTAND THE CONTENTS OF THE ABOVE-IDENTIFIED SPECIFICATION, INCLUDING THE CLAIMS, AS AMENDED BY ANY AMENDMENT REFERRED TO ABOVE;

I ACKNOWLEDGE THE DUTY TO DISCLOSE TO THE OFFICE ALL INFORMATION KNOWN TO ME TO BE MATERIAL TO PATENTABILITY AS DEFINED IN TITLE 37, CODE OF FEDERAL REGULATIONS, Sec. 1.56 (as amended effective March 16, 1992);

I do not know and do not believe the said invention was ever known or used in the United States of America before my or our invention thereof, or patented or described in any printed publication in any country before my or our invention thereof or more than one year prior to said application; that said invention was not in public use or on sale in the United States of America more than one year prior to said application; that said invention has not been patented or made the subject of an inventor's certificate issued before the date of said application in any country foreign to the United States of America on any application filed by me or my legal representatives or assigns more than twelve months prior to said application;

I hereby claim foreign priority benefits under Title 35, United States Code Sec. 119 and/or Sec. 365 of any foreign application(s) for patent or inventor's certificate as indicated below and have also identified below any foreign application for patent or inventor's certificate on this invention having a filing date before that of the application(s) on which priority is claimed:

COMBINED DECLARATION AND POWER OF ATTORNEY

Attorney's Docket No.
003300-872

COUNTRY/INTERNATIONAL	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED
Sweden	9902155-2	9 June 1999	YES X NO_
			YES_ NO_

I hereby appoint the following attorneys and agent(s) to prosecute said application and to transact all business in the Patent and Trademark Office connected therewith and to file, prosecute and to transact all business in connection with international applications directed to said invention:

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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